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Obstructive Sleep Apnea in Pregnant Women: A Review of Pregnancy Outcomes and an Approach to Management

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Abstract

Among obese pregnant women, 15%–20% have obstructive sleep apnea (OSA) and this prevalence increases along with body mass index and in the presence of other comorbidities. While Prepregnancy obesity and pregnancy-related weight gain are certainly risk factors for sleep-disordered breathing in pregnancy, but certain physiologic changes of pregnancy may also increase a woman's risk of developing or worsening OSA. While it has been shown that untreated OSA in postmenopausal women is associated with a range of cardiovascular, pulmonary, and metabolic comorbidities, a body of literature is emerging that suggests OSA may also have serious implications for the health of mothers and fetuses during and after pregnancy. In this review, we discuss the following: pregnancy as a vulnerable period for the development or worsening of OSA; the associations between OSA and maternal and fetal outcomes; the current screening modalities for OSA in pregnancy; and current recommendations regarding peripartum management of OSA.

Obesity in America has reached epidemic proportions; a generation of young people who suffer from chronic diseases previously acquired in middle age has emerged. In 2014, half of all pregnant women in the United States were overweight or obese.¹

Sleep-disordered breathing (SDB), a spectrum of conditions of increasing severity from loud snoring to obstructive sleep apnea (OSA), are often, although not always, comorbid with

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obesity. These conditions are associated with repeated partial or complete upper airway obstruction during sleep that resolves with arousal, but results in poor sleep and episodic hypoxemia and hypercarbia. The physiologic changes of pregnancy can produce or worsen SDB; up to a third of pregnant women report snoring in the third trimester.²⁻⁶ Among obese pregnant women, 15%–20% have OSA; this prevalence increases with body mass index (BMI) and other comorbidities.^{2,7-11} OSA in pregnancy is likely under-diagnosed due to a number of factors including: a lack of validated screening tools; insufficient provider awareness; and a need for greater understanding of the dynamic effects of pregnancy on OSA.¹²⁻¹⁴ In addition, OSA may be under-appreciated in premenopausal women due to older age being a known risk factor for OSA, as well as differences in the clinical presentation of women with OSA compared to men.¹⁵

While it has been shown that untreated OSA in post-menopausal women is associated with a range of cardiovascular, pulmonary, and metabolic comorbidities, a body of literature is emerging that suggests OSA may have serious implications for the health of mothers and fetuses during and after pregnancy.^{8,9,11,16-21} In this review, we will discuss the following: pregnancy as a vulnerable period for the development or worsening of OSA; the associations between OSA and adverse maternal and fetal outcomes; the current screening modalities for OSA in pregnancy; and current recommendations regarding peripartum management of OSA.

THE INTERACTION BETWEEN PREGNANCY AND SDB

While prepregnancy obesity and pregnancy-related weight gain are known risk factors for SDB in pregnancy, certain physiologic changes of pregnancy also increase a woman's risk of developing or worsening SDB. Pregnant women experience changes to the upper airway, such as mucosal hyperemia, narrowing of the oropharyngeal diameter, and increased Mallampati score, as well as decreased functional residual capacity and increased oxygen consumption that can produce or exacerbate SDB.^{22,23} In contrast, some pregnancy-related changes may be protective, such as preference for the lateral sleep position and increased respiratory rate due to hormonal changes. These changes are dynamic as pregnancy progresses.^{15,24}

There are likely 2 distinct clinical phenotypes of OSA in pregnancy: women with preexisting OSA who become pregnant and may experience worsening of the condition (chronic OSA complicated by pregnancy); and women who develop OSA related to weight gain and airway/respiratory changes of pregnancy or hypertensive disorders of pregnancy (HDP) (gestational OSA). There is some evidence that the latter condition may improve or resolve entirely after pregnancy.^{25,26} However, the term “gestational sleep apnea” has not been formally classified and has no diagnosis code. To date, the impact and progression of these 2 phenotypes during and after pregnancy have not been well described.

Pien et al² illustrated the existence of these 2 phenotypes and the progression of OSA during pregnancy. A cohort of pregnant women (n = 105, mean BMI = 33.4 kg/m²) underwent overnight, in-lab polysomnography (PSG) studies in the first and third trimesters. Significantly more women met criteria for OSA (apnea-hypopnea index [AHI] ≥ 5/h) in the

third trimester compared to the first (26.7% vs 10.5%) with age and BMI as the most significant predictors of OSA. A recent prospective study of 3702 nulliparous women who underwent home sleep testing (HST) early in pregnancy, and again midgestation, also found that more women had an AHI ≥ 5 /h later in pregnancy (8.3% vs 3.6%).¹¹ A small study of recently postpartum women showed that 20% of postpartum subjects (mean BMI = 30 kg/m²) had moderate to severe OSA (AHI >15 /h) on PSG within the first 48 hours after delivery.²⁷

SDB AND ITS ASSOCIATION WITH ADVERSE MATERNAL OUTCOMES

Several studies and 2 meta-analyses have shown that the spectrum of SDB is more common among women with other comorbidities in pregnancy: chronic hypertension (CHTN); gestational hypertension (GHTN); preeclampsia; gestational diabetes; and cardiomyopathy.^{6,9,11,18,21,28,29} Large, retrospective database studies have shown evidence of increased morbidity and mortality for pregnant women with OSA.^{9,29} These differences remained significant after controlling for obesity, an important confounder that is associated with both SDB and adverse maternal outcomes. Facco et al¹¹ recently reported an independent association between OSA in pregnancy measured by HST and the risk of developing GHTN, preeclampsia, and gestational diabetes after controlling for several covariates. However, not all studies have found a relationship between SDB and these comorbidities,^{2,30} (Table 1) and larger, prospective studies in high-risk cohorts are certainly needed. An important factor to consider when comparing these studies is how SDB is defined and determined; some studies have used symptom-based assessment tools, which have not been validated in pregnancy, instead of objective testing to define SDB.

HDP is defined by the American College of Obstetricians and Gynecologists as a spectrum of diseases that includes CHTN, GHTN, CHTN with superimposed preeclampsia, and preeclampsia/eclampsia. For the purpose of this review, we will describe the literature for CHTN separately, and refer to HDP as GHTN, superimposed preeclampsia, or preeclampsia/eclampsia.³⁵

Chronic Hypertension

In both pregnant and nonpregnant women, CHTN seems to be associated with OSA.^{16,36} In 1 study, 53% of pregnant women with CHTN reported snoring before pregnancy.²⁸ Those women who reported snoring before pregnancy had more severe OSA (diagnosed by HST in early third trimester). Moreover, women with CHTN had an increased prevalence and severity of OSA compared to normotensive controls. Three other prospective cohort studies that conducted HST in pregnancy to determine OSA status also reported a significantly greater prevalence of CHTN in the OSA (AHI ≥ 5 /h) groups.^{8,33,37} The association between OSA and CHTN was confirmed in a recent prospective study that deployed HST in over 3000 nulliparous pregnant women; the prevalence of CHTN increases with OSA severity.¹¹ CHTN in pregnancy is a known risk factor for preeclampsia; preeclampsia and related disorders are a major cause of maternal and fetal morbidity and mortality and result in significant health care expenditures.^{38,39} Pregnant women with CHTN and loud snoring are at significant risk of having comorbid OSA.

Hypertensive Disorders of Pregnancy

A number of studies have examined the relationship between HDP and symptoms of SDB during pregnancy, including snoring.^{5,40} Researchers from Sweden reported a statistically significant relationship between frequent snoring and HDP, but this study did not adjust for other risk factors for HDP.⁴¹ In a prospective study of 1673 women, pregnancy-onset snoring was associated with GHTN (adjusted odds ratio [aOR] = 2.36 [95% confidence interval {CI}, 1.48–3.77]) and preeclampsia (aOR = 1.59 [95% CI, 1.06–2.37]) after adjusting for several covariates.⁶ Some have reported that third-trimester edema is more common among women who snore frequently,^{41,42} and edema is a common physical manifestation of preeclampsia. Overall, the existing literature suggests that snoring itself, even in the absence of documented OSA, may be an important risk factor for HDP.

OSA is associated with HDP, based on an analysis of diagnosis codes recorded in the US Nationwide Inpatient Sample and the National Perinatal Information Center and 2 meta-analyses (Table 1).^{9,18,21,29} HDP is also associated with both mild and severe OSA, measured by HST after adjusting for age, BMI, CHTN, and pregnancy-related weight gain (Table 1).¹¹ In midpregnancy (22–31 weeks gestation), women with mild to moderate OSA (AHI 5–14.9/h) had 2-fold increased risk for developing HDP; this risk increased with severe OSA (aOR = 4.27 [95% CI, 1.74–10.45]).¹¹ The HDP diagnosis was established more than 2 weeks after the midpregnancy OSA assessment in 92% of cases, suggesting that HDP was not present at the time of HST for the majority of subjects. The number of women who developed HDP in this cohort was consistent with population studies (7% [n = 234] GHTN, 6% [n = 199] preeclampsia or eclampsia); 51 of the women with HDP were OSA positive.⁴³ The smaller, prospective, and retrospective studies that used objective sleep testing to classify OSA reported conflicting results with regards to HDP risk (Table 1).^{2,8,20,28,32–34} Studies that have used HDP as their inclusion criteria and then conducted objective testing for OSA have found a greater prevalence and severity of OSA among women with HDP (Table 1).^{10,28,31}

The mechanisms that link OSA to HDP have not been defined. However, some have suggested that OSA-related intermittent hypoxemia leads to HDP by causing endothelial dysfunction.²⁴ Endothelial dysfunction is implicated in the relationship between OSA and cardiovascular disease in nonpregnant adults.¹⁷ These comorbidities may be caused by repetitive cycles of hypoxemia and reoxygenation that stimulate the sympathetic nervous system and cause oxidative stress, and in turn vascular endothelial dysfunction.^{44,45} The airway edema and rostral fluid shifts associated with HDP may also worsen SDB, and these conditions may interact in a bidirectional manner.¹⁰ There is preliminary evidence that SDB in women with HDP improves in the postpartum period.^{25,26}

Notably in nonpregnant adults, treatment of OSA with continuous positive airway pressure (CPAP) improves hyper-tension and endothelial dysfunction.⁴⁶ Healthy vascular endothelium requires a homeostatic balance of angiogenic proteins (vascular endothelial growth factor and placental growth factor) and antiangiogenic proteins (soluble fms-like tyrosine kinase-1 and soluble endoglin). In adults with OSA, upregulation of antiangiogenic proteins has been associated with endothelial dysfunction.^{47,48} Interestingly, this protein imbalance is also implicated in the clinical manifestations of preeclampsia: vasoconstriction;

hypertension; and proteinuria.^{49,50} One small retrospective study provides preliminary evidence that elevated soluble fms-like tyrosine kinase-1/placental growth factor ratios are also associated with a diagnosis of OSA in the absence of preeclampsia.⁵¹ This study also detected lower serum levels of the placental peptide pregnancy-associated plasma protein A (PAPP-A) in women with OSA; this finding is usually associated with preeclampsia. Women who subsequently developed preeclampsia were excluded, and the differences remained significant. Some have proposed that OSA treatment with CPAP may play a role in the treatment of HDP.^{52–56} An Australian group has shown preliminary evidence of improved blood pressure control and increased cardiac output with CPAP in preeclamptic women with nasal airway obstruction. They also showed that AHI was significantly higher and fetal activity was reduced in preeclamptic women compared to gestational age-matched controls, and that fetal movements improved with CPAP in the preeclamptic group.^{52–54} Another group has also shown preliminary evidence that CPAP may improve blood pressure control in HDP.⁵⁵ However, Reid et al⁵⁷ randomly assigned women with GHTN to either autotitrating CPAP or nasal strips and mandibular advancement devices and found no differences in first-morning blood pressures between the 2 groups. Additional prospective studies are needed to determine whether CPAP may have a role in the treatment and prevention of HDP.

Preeclampsia imparts significant morbidity and mortality for mother and fetus, and puts women at risk for cardiovascular disease later in life.^{58–62} Some have suggested that the interaction between SDB and HDP may impart additional long-term cardiovascular risk.^{25,63}

Cardiovascular Disease

OSA is associated with cardiovascular disease among the delivering population, based on analyses of diagnosis codes recorded in the US Nationwide Inpatient Sample and the National Perinatal Information Center.^{9,29} Specifically, among women admitted antepartum or for delivery in the US Nationwide Inpatient Sample, a diagnosis of OSA was associated with cardiomyopathy (aOR = 9.0 [95% CI, 7.47–10.87]), congestive heart failure (aOR = 8.94 [95% CI, 7.45–10.73]), and pulmonary edema (aOR = 7.5 [95% CI, 4.63–12.15]).⁹ In this study, women with OSA were 5 times more likely to die during a pregnancy-related admission than women without OSA.⁹ In the National Perinatal Information Center study, after adjusting for multiple covariates, a diagnosis of OSA was associated with cardiomyopathy (aOR = 3.59 [95% CI, 2.31–5.58]), congestive heart failure (aOR = 3.63 [95% CI, 2.33–5.66]), and pulmonary edema (aOR = 5.06 [95% CI, 2.29–11.1]).²⁹ Data from the large, prospective nuMom2b Heart Health study will hopefully shed light on the impact of pregnancy on future cardiovascular health.⁶⁴

Gestational Diabetes Mellitus

Some studies have suggested a relationship between gestational diabetes and OSA, while others have not supported an association (Table 1). A 2014 meta-analysis demonstrated a significant association between gestational diabetes mellitus and SDB.²¹ Data from the US Nationwide Inpatient Sample⁹ and the National Perinatal Information Center²⁹ also showed that pregnant women with OSA were at significantly increased risk of having comorbid gestational diabetes, after controlling for obesity. However, a small, prospective study found

no differences in the AHI between the 2 groups.³⁰ The nuMom2b prospective substudy reported by Facco et al¹¹ recently demonstrated a significantly increased risk of gestational diabetes for women with mild to moderate OSA in both early and midpregnancy after adjustment for age, BMI, CHTN, and pregnancy-related weight gain (Table 1). This risk increased for women with severe OSA (AHI >15/h; aOR = 8.44 [95% CI, 1.90–37.60]).⁶⁵

We are not aware of any studies in pregnant women that have examined the effect of OSA treatment on glucose tolerance; there are modest data to suggest it may improve glycemic control in nonpregnant adults.⁶⁶ Future studies are needed to ascertain if nocturnal CPAP therapy may impact the course of these comorbid diseases in pregnant women.

OSA AND ASSOCIATIONS WITH ADVERSE FETAL AND NEONATAL OUTCOMES

Chronic sleep disturbance, nocturnal hypoxemia, and the neuroendocrine alterations associated with OSA may impact fetal growth and well-being, based on several preliminary studies. However, the results and outcomes reported of retrospective and prospective studies have been inconsistent. The available studies that used objective measures to define OSA are summarized in Table 2. This is an area that warrants future research.

Fetal Heart Rate Abnormalities

One of the first descriptions of OSA in pregnancy was a small case series published in 1978 that described fetal heart rate (FHR) abnormalities during witnessed maternal apneic events.⁶⁸ Thirty years later, 2 prospective studies conducted FHR monitoring with simultaneous maternal PSG to observe the effect of maternal apneas and oxygen desaturations on FHR.^{69,70} Sahin et al⁶⁹ reported FHR decelerations during maternal apneic episodes in 3 women with OSA diagnosed by PSG, but the study was small and did not characterize the FHR decelerations or correlate them with maternal respiratory events. A study by Olivarez et al⁷⁰ conducted simultaneous FHR monitoring with portable PSG and found no association between apnea episodes and FHR abnormalities among 20 women with AHI >5/h.

Fetal Growth Restriction

Interest in a clinically observed association between maternal OSA and poor fetal growth also grew out of early case reports.^{71–73} Pamidi et al²¹ reviewed 7 studies that examined the association between SDB and low neonatal birth weight, and reported a significant association between maternal SDB and low infant birth weight (Table 2). Five of the 7 studies included were based on symptom-based assessments of SDB. Ding et al⁶⁷ analyzed 11 studies that reported fetal growth restriction (FGR; as opposed to neonatal birth weight) outcomes for women with SDB and found a modestly increased risk of FGR for women with SDB. Seven of the 11 studies analyzed defined SDB using symptoms, while 4 studies used objective testing.

Obesity, advanced maternal age, and preeclampsia are all associated with both SDB and FGR; common underlying pathways may connect these comorbidities.^{2,7,11,74} Studies of pregnant women who live at high altitude with chronically low arterial oxygen partial

pressures demonstrate an increased risk of preeclampsia and FGR.^{75,76} To our knowledge, no studies in pregnant women with OSA have investigated the effects of repetitive, nocturnal exposure to hypoxemia in this disease state.^{77,78} In vitro and animal studies suggest that oxygen tension plays a crucial role in the early development of the placenta, and that alterations in oxygen tension may predispose to the placental pathology seen in preeclampsia and FGR.^{79–82} Hypoxia-inducible factors-1 and 2 (HIF-1 and 2) are transcription factors involved in the cellular response to low oxygen tension.⁸³ HIF-1 and 2 are overexpressed in the placentas of women living at high altitude, women with preeclampsia, and rats with growth-restricted fetuses.^{84–86} HIFs may connect OSA with hyper-tension in nonpregnant adults, as mediators of hypoxemia, sympathetic nervous system activation, oxidative stress, and endothelial dysfunction.⁸⁷

A recent study showed that women at higher risk for SDB as determined by sleep questionnaires had neonates with shorter telomere lengths in their DNA obtained from cord blood samples.⁸⁸ Shorter telomere lengths are associated with accelerated aging and age-related disease, and have also been observed in adults with OSA.^{88,89}

CURRENT SCREENING MODALITIES FOR OSA IN PREGNANCY

OSA is under-appreciated and under-diagnosed in pregnancy due to a number of factors including a lack of validated screening tools and the complexity of diagnosis protocols. Overnight, in-lab PSG is the gold standard for diagnosis of OSA, but is expensive, and backlogs can delay PSG completion for up to several months.^{14,90} A number of investigators have tried to validate established OSA screening questionnaires in parturients or to create new tools.^{7,37,70,91} In pregnancy, these screening tools are associated with a high false referral rate for PSG.⁹² The screening tools that have been tested against HST are summarized in Table 3.^{7,37,70,91} HST is emerging as a reliable, convenient, and cost-effective method of screening high-risk patients for OSA,^{93–95} and has been used in a number of studies of pregnant women. Some HST devices have been validated in pregnant populations.^{7,8,96} While HST tends to underestimate the severity of OSA, it is likely to detect moderate to severe OSA, particularly when mild-range AHI scores ($< 5/h$) are considered the threshold for further investigation.⁹⁷ These devices are being used in clinical practice to screen other patient populations at moderate to high risk for OSA when diagnosis and treatment are time sensitive.⁹⁸

While validated OSA screening tools for pregnant women are limited, maternity care providers should use clinical judgment or institutional guidelines to consider sleep medicine referral and anesthesiology consultation when one or more of the following risk factors is present: morbid obesity; neck circumference greater than 40 cm; history of difficult airway; CHTN; history of GHTN; loud and frequent snoring; observed apneas; or daytime somnolence in situations where sleepiness normally does not occur.^{2,7,28,37,99} Adding a serum bicarbonate level >28 mmol/L to a score ≥ 3 on the STOP-BANG questionnaire improved the specificity of the tool in nonpregnant subjects from 37% to 85% for all OSA severity.¹⁰⁰ This is an area that warrants further study in pregnant subjects as serum bicarbonate levels are normally lower in pregnancy, and elevated levels would then be even more concerning for chronic carbon dioxide retention.

All obstetric patients should be assessed for OSA, to screen for new-onset or a medical history of SDB.⁹⁹ There is no literature to support the optimal timing of this screening. In our practice, we recommend prenatal OSA screening between 12 and 18 weeks to allow adequate time for evaluation and possible treatment early in pregnancy. In cases of known OSA with treatment nonadherence, reestablishment of treatment should be encouraged and supported. If OSA is suspected, patients should be referred to a sleep medicine physician for evaluation and treatment, usually with autotitrating CPAP. Autotitrating CPAP is useful as airway obstruction can worsen as pregnancy progresses and improve postpartum. The sleep medicine provider can follow data from the CPAP machine after delivery to determine if long-term CPAP is needed after the patient's physiology returns to the nonpregnant state. Patients diagnosed with moderate to severe OSA may have comorbid pulmonary hypertension, and echocardiography during pregnancy should be considered. If patients present in the third trimester and are suspected to have OSA, we refer them for sleep medicine consultation, despite the fact that the appointment may occur postpartum. OSA has implications for a woman's health beyond pregnancy, and should be addressed regardless of pregnancy status.

Enthusiasm for OSA screening among obstetricians and anesthesiologists has been tempered by the lack of studies to support whether treatment of OSA in pregnancy could modify the adverse pregnancy outcomes associated with OSA, as well as the practical limitations of the availability of sleep medicine referrals and patient cooperation with diagnosis and treatment. As additional data become available regarding the adverse outcomes associated with OSA in pregnancy, screening algorithms that target high-risk women will need to be developed and validated.

PERIPARTUM MANAGEMENT OF OSA

Peripartum morbidity and mortality are increased for women with OSA^{9,29}; OSA and obesity were identified as important risk factors for anesthesia-related maternal mortality in a statewide analysis of maternal deaths.¹⁰¹ While specific guidelines regarding the management of OSA during pregnancy are lacking, the American Society of Anesthesiologists' (ASA's) practice guidelines for the perioperative management of patients with OSA provide guidance that can be applied to this population.^{102,103}

Studies have not yet shown whether OSA treatment may improve pregnancy outcomes associated with OSA, but the ASA and Society for Anesthesia and Sleep Medicine guidelines are clear that for surgical patients, preoperative evaluation and treatment of OSA is optimal. Pregnant women with OSA are at greater risk for requiring cesarean delivery, and should be treated like other presurgical patients.¹⁸ Patients with OSA should be sent for consultation with an anesthesiologist in advance of their delivery to review available medical records regarding OSA severity and treatment and history of difficult airway or other perioperative complications, as well as for airway examination and to discuss peripartum recommendations. Patients with OSA should be encouraged to bring their CPAP machine to the hospital and wear it during sleep in the peripartum admission. A recent study of bariatric surgery patients showed that CPAP mitigated the respiratory depressant effects of opioids for postoperative pain, and improved AHI to baseline.¹⁰⁴ We recommend anesthesia

consultation in the early third trimester to allow time for additional studies or consultations to be obtained if necessary, and given the increased risk of early delivery in this population. In the absence of current guidelines for the peripartum diagnosis and management of OSA, institutions should develop their own interdisciplinary, clinical care pathways to optimize the care of these high-risk patients.

Gastroesophageal reflux disease (GERD) and OSA are often comorbid; obesity is thought to be the main mediating factor between the 2 diseases.¹⁰⁵ GERD symptoms are common in pregnant women, regardless of body weight, due to several physiologic changes of pregnancy, including decreased lower esophageal sphincter tone.¹⁰⁶ For women with SDB, nocturnal GERD symptoms may further disrupt sleep and contribute to daytime sleepiness. The frequency of GERD symptoms in pregnant women significantly correlates with prepregnancy BMI and BMI at delivery.¹⁰⁶ We are not aware of any studies on the effect of CPAP therapy on GERD symptoms in pregnant women. However, in nonpregnant patients, adherence to CPAP therapy may actually decrease GERD symptoms.¹⁰⁷ Some patients on CPAP therapy do experience aerophagia, introduction of air into the esophagus, which results in gastrointestinal discomfort and belching. Aerophagia may be related to decreased lower esophageal sphincter tone, which could be of concern in pregnant patients on CPAP.^{108,109} Whether CPAP also increases the risk of aspiration in pregnant women is of theoretical concern, but there is no literature reporting increased complications with CPAP in pregnant women.¹¹⁰

Sedating antiemetics, anxiolytics, and sleep aids should be avoided or used with caution in patients with SDB, particularly if combined with opioids. Patient-controlled systemic opioids should also be used judiciously, and continuous infusions avoided. The ASA guideline recommends that patients with known and suspected OSA should be monitored postoperatively with continuous pulse oximetry. While there are no obstetric-specific guidelines, those with known or suspected OSA should be monitored with continuous pulse oximetry in the labor or recovery room and receive supplemental oxygen until they maintain their baseline oxygen saturations on room air. CPAP should be added during periods of sleep. Patients with known or suspected OSA should continue to be monitored with continuous pulse oximetry until they are no longer at risk of postoperative respiratory depression.¹⁰² In postpartum settings where this is not feasible and for all patients with comorbid cardiopulmonary disease, monitoring in an intensive care or step-down unit should be strongly considered. Patients with witnessed apneas and oxygen desaturations intra- or postoperatively should not be discharged to an unmonitored setting. A recent study in surgical patients showed that patients deemed at moderate to high risk of OSA by STOP-BANG screening on the day of surgery, but previously undiagnosed, had increased postoperative respiratory interventions, hospital use, and 30-day all-cause mortality compared to surgical patients with a known OSA diagnosis.¹¹¹ This evidence supports early objective screening and that OSA peripartum/perioperative protocols should extend to patients with suspected and known OSA, but studies and guidelines in obstetric patients are needed.

Multimodal postoperative analgesia with nonsteroidal anti-inflammatory agents and acetaminophen are recommended when possible to decrease the need for opioids and their

associated risks of sedation and hypoventilation; trans-versus abdominis plane (TAP) block, local anesthetic wound catheters, and neuraxial techniques may be considered for postoperative analgesia when appropriate or in centers that do not use neuraxial morphine (NM).^{112,113} TAP blocks/catheters have not been shown to provide additional benefit when NM is administered, and they can be technically challenging in the morbidly obese.¹¹⁴ A recent study of 100 µg intrathecal morphine (ITM) versus 0.2% ropivacaine wound catheter infiltration showed no difference in the duration of postoperative analgesia between the 2 approaches, but morphine consumption was lower with ITM.¹¹² However, data comparing local anesthetic wound catheters with ITM for postcesarean delivery pain are limited, and an earlier study found that ITM was superior.¹⁰³ Compared to TAP blocks, which provide only incisional pain relief, wound catheters placed below the fascia have a potential ability to provide some degree of visceral pain relief. The risk-benefit of neuraxial techniques for postoperative analgesia in obstetric patients is limited by the emphasis on early ambulation and venous thromboembolism prophylaxis.

Controversy has surrounded the safety of NM in parturients with or at risk for OSA given the theoretical risk of rostral spread and respiratory depression. There are little data on the incidence of respiratory depression in the obstetric population, but reported incidence ranges between 0% and 0.9%.^{115–118} However, we are not aware of any studies that have been able to establish the true risk of respiratory depression with NM in morbidly obese or OSA patients. A retrospective study of 5036 women (mean BMI = 33.7 kg/m²) who received NM for cesarean delivery found no instances of respiratory depression requiring rapid response team involvement or naloxone administration.¹¹⁹ A recent study of postcesarean delivery patients who received NM showed that a significant number of healthy women (median BMI = 29 kg/m² [27–32 interquartile range]) had sustained hypercapnia (measured by a transcutaneous carbon dioxide monitor).¹²⁰ The only predictive factor for hypercarbia was elevated baseline transcutaneous carbon dioxide level; age, BMI, total opioid consumption, and STOP-BANG scores did not correlate with hypercarbia. The study group was not compared to women who did not receive NM, and experienced no clinically significant events, so it is difficult to draw conclusions from this regarding patient management. Further studies using continuous monitoring of ventilation and oxygenation of postpartum patients and comparing neuraxial opioids with intravenous patient-controlled opioid analgesia are needed.

Currently, many clinicians feel that the risk of oversedation and respiratory depression in obese and OSA patients might be greater with systemic opioids than with appropriate doses of NM given the low incidence of respiratory depression requiring intervention that has been reported in the literature, and therefore recommend using NM with appropriate monitoring, care protocols, and multimodal analgesia to decrease breakthrough pain. Some centers monitor continuous pulse oximetry for 24 hours in obstetric patients who have received NM; others conduct hourly monitoring of sedation, respiratory rate, and pulse oximetry every 1 hour for 12 hours, and then every 2 hours for the next 12 hours as recommended by the current ASA guidelines.¹²¹ In centers with electronic medical record systems, we recommend a dedicated order set to alert providers of the administration of NM (for 24 hours from administration), to provide warnings if other sedating drugs are ordered, and to provide emergency naloxone orders as needed.

CONCLUSIONS

Emerging data suggest that women with OSA in pregnancy are at higher risk of pregnancy- and anesthesia-related complications. A small number of studies suggest that OSA may affect a woman's offspring as well. OSA has been associated with chronic and pregnancy-induced hypertensive disorders; both are associated with higher rates of preterm birth. SDB is under-appreciated and under-diagnosed among premenopausal women likely due to a number of factors including: insufficient provider awareness of risk factors; a lack of validated screening tools; limited understanding of the dynamic effects of pregnancy on OSA across trimesters; and practical challenges that limit the availability of in-lab, overnight PSG testing.^{14,90} Despite concerns about the potential adverse impact of OSA on mothers and their offspring, a reliable screening tool for OSA in pregnancy has not been developed. HST to ascertain OSA risk may be a viable screening tool for high-risk women, but further studies are needed to confirm the feasibility and cost-effectiveness of this approach. Data regarding the impact of OSA treatment on adverse pregnancy outcomes are still needed. However, identifying OSA early in a woman's life may have positive effects on long-term health outcomes after pregnancy; pregnancy may be the best opportunity for early detection. If OSA treatment is shown to reduce the risk of HDP, this could potentially reduce a woman's risk of future cardiovascular and renal disease, as these diseases are more prevalent in women who have had HDP.^{122,123}

Pregnancy-specific practice guidelines for the detection and management of OSA have not yet been developed and the data to inform them are needed. In the absence of these recommendations, guidance can be drawn from the Society for Anesthesia and Sleep Medicine and ASA's practice guidelines. Novel monitoring techniques may inform future studies to ascertain the true risk of NM administration in high-risk parturients. Nonopioid-based analgesic modalities should be encouraged in this population.

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Table 1. Selected Studies of HDP and Gestational Diabetes Risk in Women With Obstructive Sleep Apnea That Included Objective Sleep Testing

Authors	Study Type	Number of Mothers Studied	Inclusion Criteria	OSA Status of Mother	Gestational Age at Time of Sleep Testing (wk)	GHTN	Preeclampsia	HDP	Eclampsia	GDM
Bisson et al ³⁰	P	52	GDM; nondiabetic C	HST	24–33	-	-	-	-	No association
Bouffely et al ²⁹	R	1,577,632	OSA in pregnancy	ICD code	Varied	1.7 (1.4–2.0)	2.22 (1.9–2.5)	-	2.95 (1.1–8.0)	1.5 (1.3–1.7)
Champagne et al ³¹	P	50	GHTN; normotensive C	PSG; AHI 15	Varied	7.5 (3.5–16.2)	-	-	-	-
Chen et al ²⁰	R	791	-	ICD code	Varied	3.2 (2.1–4.7)	1.6 (2.2–11.3) ^a	-	-	1.6 (1.1–2.5)
Facco et al ³²	R	143	PSG in hospital records	AHI 5 on PSG	Varied	2.9 (1.1–7.9) ^b	<i>e</i>	<i>b</i>	<i>b</i>	<i>b</i>
Facco et al ³³	P	188	High of risk preeclampsia ^e	AHI 5 on HST	6–20	-	No association	-	-	Mild OSA: 1.5 (0.4–6.0) Moderate–severe OSA: 3.6 (0.6–21.8)
Facco et al ¹¹	P	3705	Nulliparity, singleton	AHI 5 on HST	28–37	-	No association	-	-	-
Louis et al ³⁴	R	171	OSA in pregnancy; BMI-matched C	PSG; no PSG testing of C	-	-	1.94 (1.07–3.5)	1.5 (0.9–2.3) ^e	-	3.5 (2.0–6.2)
Louis et al ⁸	P	182	BMI 30 kg/m ²	AHI 5 on HST	22–31	-	2.0 (1.2–3.2)	1.7 (1.2–2.5)	-	2.8 (1.6–4.8)
Louis et al ⁹	R	55,781,965 discharges	-	ICD code	-	1.3 (1.1–1.5)	2.5 (2.2–2.9)	-	5.4 (3.3–8.9)	1.9 (1.7–2.1)
O'Brien et al ²⁸	P	67	HDP ^e ; normotensive C	Portable PSG; AHI 5	Varied	-	-	2.0 (1.4–2.8) ^e	-	-
Pamidi et al ²¹	MA	16 studies included	-	PSG	Varied	-	-	2.3 (1.1–4.5)	-	Not pooled

Adjusted Odds Ratio (95% Confidence Interval)

Authors	Study Type	Number of Mothers Studied	Inclusion Criteria	OSA Status of Mother	Gestational Age at Time of Sleep Testing (wk)	GHTN	Preeclampsia	HDP	Eclampsia	GDM
Pien et al ²	P	105	Stratified by BMI	In-lab PSG	8–14	-	-	3.1 (2.3–4.3) ^f	-	2.8 (2.0–4.0)
Reid et al ¹⁰	P	60	GHTN; normotensive C	PSG	32	8.31 (2.07–33.43)	-	-	-	-
Xu et al ¹⁸	MA	5 studies included	-	In-lab PSG, HST or symptom based	Varied	-	2.0 (1.3–2.9)	-	-	1.4 (0.6–3.2)
		3 studies included		Excluded symptom based	Varied		2.3 (1.8–3.2)			

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; C, controls; GDM, gestational diabetes mellitus; GHTN, gestational hypertension; HDP, hypertensive disorders of pregnancy; HST, home sleep test; HTN, hypertension; ICD, International Classification of Diseases; MA, meta-analysis; OSA, obstructive sleep apnea; P, prospective, observational; PSG, polysomnography; R, retrospective, population-based, cross-sectional analysis.

^aComposite outcome of preeclampsia and eclampsia.

^bComposite outcome for moderate to severe OSA included GHTN, preeclampsia, severe preeclampsia, eclampsia, and gestational diabetes.

^cHigh risk for preeclampsia defined as having either BMI ≥ 30 kg/m², chronic hypertension, preeclampsia, history of preeclampsia, and/or twin gestation.

^dHDP composite outcome included: mild, severe, and superimposed preeclampsia and eclampsia, plus antepartum GHTN.

^eHypertensive disorders composite inclusion criteria: chronic hypertension, GHTN, or preeclampsia.

^fComposite outcome included GHTN or preeclampsia.

Table 2.

Fetal and Neonatal Complications in Studies of Parturients With Obstructive Sleep Apnea

Author	Study Type	Number of Mothers Studied	OSA Status of Mother	Preterm Birth (<32 wk)	Preterm Birth (<37 wk)	5-min Apgar <7	NICU/SN	Hyperbilirubinemia	Perinatal Death	LGA	SGA	LBW
Bin et al ^{19a}	R	OSA: 519 C; 636,227	ICD code	-	1.5 (1.2-1.8) (<36 wk)	1.6 (1.1-2.4)	1.3 (1.1-1.4)	-	1.7 (0.9-3.3)	1.3 (1.0-1.6)	0.8 (0.6-1.1)	-
Chen et al ²⁰	R	OSA: 791 C; 3955	ICD code	-	2.3 (1.8-3.0)	10.1 (3.5-29.7)	-	-	-	-	1.3 (1.1-1.7)	1.8 (1.3-2.4)
Ding et al ⁶⁷	SR	24 studies analyzed	Heterogeneous in included studies	-	1.6 (0.9-2.8)	-0.01 (-0.1-0.09)	3.4 (1.2-9.3)	-	-	-	1.4 (1.2-1.7)	1.9 (1.4-2.5)
Louis et al ⁹	R	55,781,965 overall OSA rate: 3/10,000 (95% CI, 2.8-3.2)	ICD code	-	1.2 (1.1-1.4) ^b	-	-	-	1.0 (0.7-1.5) ^c	-	1.2 (1.0-1.5) ^d	-
Louis et al ⁸	P	OSA: 26 C; 135	AHI 5 HST	0.9 (0.1-8.9)	0.6 (0.2-2.2)	-	3.4 (1.2-9.3)	3.6 (1.4-9.8)	-	-	-	-
Pamidi et al ²¹	SR	7 studies analyzed	Heterogeneous in included studies	-	-	-	-	-	-	-	-	1.4 (1.1-1.7)
Pien et al ²	P	105	In-lab PSG	-	0.8 (0.2-3.8)	-	-	-	-	-	-	1.7 (0.4-7.3)

All studies include objective methods to define obstructive sleep apnea; meta-analyses include both symptom-based and objective assessments.

Abbreviations: C, controls; CI, confidence interval; HST, home sleep test; ICD, International Classification of Diseases; LBW, low birth weight <2500 g; LGA, large for gestational age; NICU, neonatal intensive care unit; OSA, obstructive sleep apnea; P, prospective, observational; PSG, polysomnography; R, retrospective, population-based, cross-sectional analysis; SCN, special care nursery; SGA, small for gestational age; SR, systematic review.

^a Adjusted relative risk (95% CI) reported by Bin et al.¹⁹

^b Reported as “Early Onset Delivery (ICD-9CM 644.2x)” by Louis et al.⁹

^c Reported as “Stillbirth (ICD-9CM 656.4x, V27.x)” by Louis et al.⁹

^d Reported as “Poor fetal growth (ICD-9CM 656.5x)” by Louis et al.⁹

Table 3.

Key Studies of Screening Tools for Sleep-Disordered Breathing in Pregnant Women

Author	Study Type	Number of Mothers Studied	OSA Status of Mother and Timing of Screening	Berlin Questionnaire	Epworth Sleepiness Scale		STOP	STOP-BANG	ASA Checklist
						Sensitivity/Specificity			
Facco et al ⁷	P	114	AHI 5 on HST between 6 and 20 wk gestation	39%	68%	36%	77%	-	-
Lockhart et al ³⁷	P	248	AHI 5 on HST; third trimester	73%	61%	57%	58%	63%	76%
Olivarez et al ⁷⁰	P	100	AHI 5 on HST; third trimester	35%	64%	-	-	-	-
Tantrakul et al ⁸⁰	P	72, 23, first T 24, second T 25, third T	AHI 5 on HST; each trimester	First T: 29% Second T: 75% Third T: 63%	First T: 69% Second T: 94% Third T: 100%	-	-	-	-
								First T: 57% Second T: 63% Third T: 63%	First T: 88% Second T: 94% Third T: 88%

Abbreviations: AHI, apnea-hypopnea index; ASA, American Society of Anesthesiologists; HST, portable home sleep test; HTN, hypertension; OSA, obstructive sleep apnea; P, prospective, observational cohort; T, trimester.